JACC Vol. 22, No. 6
November 15, 1993:1711–7

Comparison of Number of Extrastimuli Versus Change in Basic Cycle Length for Induction of Ventricular Tachycardia by Programmed Ventricular Stimulation

DAVID S. W. HO, MBBS, FRACP, MARK J. COOPER, MBBS, PhD, FRACP, FACC, DAVID A. B. RICHARDS, MD, FRACP, FACC, JOHN B. UTHER, MD, FRACP, FACC, ALEX S. B. YIP, MBBS, MRCP, DAVID L. ROSS, MBBS, FRACP, FACC

Sydney, New South Wales, Australia

Objectives. **The purpose of this study was to examine the effects of varying basic cycle lengths in a programmed stimulation protocol if up to seven extrastimuli were available at each basic cycle length.**

Background. **There is no uniformly accepted protocol for induction of ventricular tachycardia. Most protocols limit the number of extrastimuli to two or three but use several basic cycle lengths.**

Methods. **Twenty-eight patients with coronary artery disease and documented spontaneous sustained ventricular tachycardia or ventricular fibrillation were studied. In the absence of antiarrhythmic drugs, each patient underwent three inductions of ventricular tachycardia/ventricular fibrillation using sinus rhythm or right ventricular pacing at 600 or 400 ms as the basic cycle length. Up to seven extrastimuli were allowed at each basic cycle length.**

Results. **The maximal yield of clinical tachycardia (96%) was identical for each basic cycle length and was achieved using a maximum of seven, five and four extrastimuli for sinus rhythm and 600 and 400 ms, respectively. A basic cycle length of 400 ms required fewer extrastimuli (2.4 ± 0.7) to induce ventricular tachycardia/ventricular fibrillation than did 600 ms (2.7 ± 1.1, $p = 0.014$) or sinus rhythm (3.4 ± 1.2, $p < 0.001$). There was no significant difference in the cycle lengths of the induced ventricular tachycardia, incidence of induced ventricular fibrillation or requirement for direct current countershock.**

Conclusions. **The use of an adequate number of extrastimuli obviates the need for multiple basic cycle lengths for induction of ventricular tachycardia and does not increase induction of unwanted ventricular fibrillation. If only one basic cycle length is used, the ease of inducibility can be quantified in terms of the number of extrastimuli required. Fewer extrastimuli were required for induction of ventricular tachycardia if a basic cycle length of 400 ms was used. These data favor the use of ventricular pacing at a basic cycle length of 400 ms with up to at least four extrastimuli as the standard stimulation protocol for induction of ventricular tachycardia.**

(J Am Coll Cardiol 1993;22:1711–7)

Programmed ventricular stimulation is commonly used for a definitive diagnosis of ventricular tachycardia, to guide selection of antiarrhythmic drug therapy and to assess patients before and after implantation of antitachycardia devices or surgery for ventricular tachycardia (1). Each stimulation protocol has four main components (the site of stimulation, the current of stimulation, the basic cycle length and the number of extrastimuli). It is generally agreed that varying the pacing site or increasing the pacing current is not as effective as using different basic cycle lengths or adding extrastimuli for increasing the yield of inducible ventricular tachycardia (2–7). However, it is controversial which of the last two variables is more potent for inducing tachycardia without increasing the risk of inducing polymorphic ventricular tachycardia or ventricular fibrillation. Thus, when tachycardia is not induced with the initial protocol in patients with documented spontaneous ventricular tachycardia or ventricular fibrillation, many centers repeat stimulation at a different basic cycle length, whereas others apply additional extrastimuli. Although this issue has been examined previously, there are potential flaws in these studies.

All studies to date comparing the effect of different basic cycle lengths and number of extrastimuli have been limited to a maximum of one (8), two (4) or three extrastimuli (9). The sequence of delivery of the various basic cycle lengths was not randomized (4,8,9). One study was retrospective (4). All of these studies have included some patients taking antiarrhythmic drugs. In some studies, patients were excluded if their induced tachycardia required direct current countershock so that only patients with hemodynamically well tolerated ventricular tachycardia were included (9–11). The shortest coupling interval of each extrastimulus was

From the Cardiology Unit, Westmead Hospital, Westmead, Sydney, New South Wales, 2145, Australia. Dr. Ho is the recipient of a National Health and Medical Research Council Medical Postgraduate Research Scholarship (Grant 908128), Canberra, Australian Capital Territory, Australia.

Manuscript received January 25, 1993; revised manuscript received May 26, 1993, accepted June 9, 1993.

Address for correspondence: Dr. David L. Ross, Cardiology Unit, Westmead Hospital, Westmead, Sydney, New South Wales, 2145, Australia.

©1993 by the American College of Cardiology

0735-1097/93/$6.00

often restricted to 200 ms (9,12). The effect of repeating the same stimulation protocol with the same basic cycle length at the same site on increasing the inducibility of tachycardia, as described by Cooper et al. (13), was not taken into account in these studies. Finally, patients with tachycardia of several different etiologies were included.

The present study examined the effects of varying basic cycle lengths on the inducibility of ventricular tachycardia if up to a maximum of seven extrastimuli were available at each basic cycle length. The basic cycle lengths tested were sinus rhythm and ventricular pacing at 600 and 400 ms. The strengths of this study were prospective design, randomized order of application of each basic cycle length and use of a relatively large number of extrastimuli at each basic cycle length. Administration of all antiarrhythmic drugs was discontinued for at least 1 week before the electrophysiologic study, and each patient underwent three inductions of ventricular tachycardia/ventricular fibrillation irrespective of the need for direct current countershock. There was no restriction on the shortest coupling interval of each extrastimulus, and each extrastimulus coupling interval was applied three times before decrementing to minimize the effect of repetition alone (13).

Methods

Patients. Patients were entered into the study if: 1) documented *spontaneous* sustained ventricular tachycardia or cardiac arrest had occurred in the absence of an acute infarction, ischemia or metabolic disturbance; 2) electrophysiologic study was planned for diagnosis and management; 3) previous myocardial infarction was documented by history, electrocardiogram (ECG), coronary angiography and left ventriculography; and 4) written informed consent was given. Thirty consecutive patients who met these entry criteria were studied. Two patients were later excluded because of failure to complete all three baseline inductions of ventricular tachycardia or fibrillation. One of these withdrew consent after two inductions of ventricular tachycardia, the other required exceptionally prolonged resuscitation after the initial induction of ventricular tachycardia, and it was considered unwise to perform more baseline inductions. The clinical characteristics of the 28 patients who completed the study protocol are shown in Table 1. The clinical arrhythmia was monomorphic ventricular tachycardia in 23 patients and ventricular fibrillation in 5. Administration of all antiarrhythmic drugs (including verapamil and beta-adrenergic blocking agents) was discontinued for 7 days before the studies. One patient was studied 7 days after a single 300-mg oral dose of amiodarone, given before transfer from a peripheral hospital. Amiodarone therapy was discontinued 24 days before the study in another patient who had been taking this agent on a long-term basis.

Definitions. *Sustained monomorphic ventricular tachycardia* was defined as ventricular tachycardia with a constant morphology in Frank surface ECG leads X, Y and Z; a cycle length of ≥200 ms; and a duration of at least 10 s. All sustained episodes of ventricular fibrillation, ventricular flutter (fast monomorphic ventricular tachycardia with a cycle length of <200 ms) or polymorphic ventricular tachycardia were grouped as *sustained polymorphic ventricular tachycardia/ventricular fibrillation*. Induced sustained polymorphic ventricular tachycardia/ventricular fibrillation was considered *clinical* if the patient had a previous clinical ventricular tachyarrhythmia of the same type. All induced sustained polymorphic ventricular tachycardia/ventricular fibrillation was considered an *unwanted arrhythmia* if sustained monomorphic ventricular tachycardia had been the clinically documented arrhythmia, and there was no history of previous ventricular fibrillation.

Table 1. Clinical Characteristics of Patients

	No.
Men/women	20/8
Age (yr)	66 ± 8 (range 39 to 80)
Documented clinical arrhythmia	
Monomorphic VT	23
VF	5
Anterior MI	14
Inferior MI	10
Anterior + inferior MI	4
Previous CABG	11
Left ventricular ejection fraction (%)	32 ± 13 (range 15 to 56)

Values presented are mean value ± SD or number. CABG = coronary artery bypass graft, MI = myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

The *effective refractory period* was defined as the longest extrastimulus coupling interval at which there was failure of constant ventricular capture. If tachycardia was induced by the first extrastimulus, no effective refractory period was established for that extrastimuius. If tachycardia was induced by the nth extrastimulus, the effective refractory periods for extrastimuli 1 to n − 1 were established but not for the nth extrastimulus.

Study protocol. The study protocol was approved by the Research and Ethics Committees of the Western Sydney Area Health Service. The basic cycle lengths tested were sinus rhythm and right ventricular pacing at 600 and 400 ms. These three basic cycle lengths were applied in a predetermined order for each patient at the single electrophysiologic study to ensure that there was no biased preference for one basic cycle length to occur as the first, second or third induction. A table of random numbers was used for randomization.

Studies were performed in the postabsorptive, sedated state (diazepam, 10 mg given orally 1 h before study). Quadripolar electrode catheters were positioned in the right atrial appendage and the right ventricular apex and a tripolar electrode catheter at the His bundle region. Three orthogonal ECG leads (Frank leads X, Y and Z) and the intracardiac electrograms were recorded with a Siemens-Elema Mingograf 804 recorder. Programmed stimulation was performed

Table 2. Sequence of Application of Basic Cycle Lengths, Incidence of Induced Polymorphic Ventricular Tachycardia or Ventricular Fibrillation and Requirement for Direct Current Countershock

	Basic Cycle Length				
	Sinus Rhythm (704 ± 168) ms*	600 ms (565 ± 49) ms*	400 ms (400 ± 0) ms*	PMVT/ VF	DC Countershock
1st application	10	10	9	3	8
2nd application	9	9	9	5	9
3rd application	9	9	10	4	7
PMVT/VF	4	4	4		
DC countershock	10	7	7		

*Mean value ± SD in ms. Values presented are number of patients. DC = direct current; PMVT/VF = sustained polymorphic ventricular tachycardia and ventricular fibrillation, as defined in the text.

at the right ventricular apex using a WPI (World Precision Instruments) stimulator. Pacing stimuli were 2 ms in duration and twice diastolic threshold current intensity. Basic drive trains consisted of 8 beats and were separated by pauses of 3 s. Delivery of extrastimuli began at an initial coupling interval of 300 ms. Each extrastimulus coupling interval was repeated three times before it was decreased by 10 ms to maximize the yield of inducible ventricular tachycardia for each extrastimulus, as shown previously (13). If repetition had not been used, a shorter coupling interval or an additional extrastimulus would have been required in two thirds of the studies (13). When the right ventricular effective refractory period was reached, the extrastimulus coupling interval was increased by 10-ms increments until stable ventricular capture was obtained. A second extrastimulus was then introduced and decremented in the same manner as the first extrastimulus. Further extrastimuli were added in the same manner until sustained ventricular arrhythmia was induced or a maximum of seven extrastimuli had been delivered.

The end points of stimulation were induction of sustained ventricular tachycardia or ventricular fibrillation. Induction of nonsustained ventricular arrhythmia of <10-s duration was not an end point. Sustained ventricular tachycardia and ventricular fibrillation were terminated by overdrive pacing or direct current countershock. After either arrhythmia was terminated, the patient was given a 10-min rest period before the next induction was attempted at a different basic cycle length. At the new basic cycle length, the full stimulation protocol was begun anew, starting with the first extrastimulus.

Statistics. Data are expressed as mean value ± SD. Analysis of variance was used to compare the cycle lengths of induced ventricular tachycardia at the different basic cycle lengths. The Wilcoxon paired test was used to compare the mean number of extrastimuli required to induce ventricular tachycardia at the different basic cycle lengths. Intention to treat analysis was used when the actual pacing cycle length varied from the randomized value in some cases. The chi-square test was used to test association between frequency of countershock requirement and basic cycle length. A p value < 0.05 was considered statistically significant.

Results

Basic cycle length. The randomized sequence of the basic cycle lengths is shown in Table 2. When 600 ms was the intended basic cycle length, 11 patients underwent pacing at a cycle length of 450 to 580 ms because of underlying sinus tachycardia. When 400 ms was the intended basic cycle length, pacing at 400 ms was successfully performed in all patients. Thus, the mean cycle lengths of the drive chain were 704 ± 168 ms for sinus rhythm and 565 ± 49 and 400 ± 0 ms, respectively, when 600 or 400 ms was the intended basic cycle length.

Number of extrastimuli. The number and coupling intervals of extrastimuli required to induce tachycardia in each patient are shown in Table 3. A basic cycle length of 600 ms required significantly fewer extrastimuli to induce tachycardia than did one using sinus rhythm as the basic cycle length (2.7 ± 1.1 vs 3.4 ± 1.2, $p < 0.001$). In turn, a basic cycle length of 400 ms required significantly fewer extrastimuli to induce tachycardia than did one using 600 ms as the basic cycle length (2.4 ± 0.7 vs 2.7 ± 1.1, $p = 0.014$). Ventricular tachycardia was always induced with an equal or smaller number of extrastimuli by a shorter basic cycle length than by a longer basic cycle length, with only one exception among the 84 comparisons (sinus rhythm vs. 600 ms in Patient 14).

Yield of tachycardia. The cumulative yield of clinical tachycardia for each basic cycle length and the number of extrastimuli required are shown in Figure 1. Several points are apparent. 1) At any given number of extrastimuli up to four, the yield of tachycardia was higher with a shorter basic cycle length. 2) If an adequate number of extrastimuli was used, the maximal yield of ventricular tachycardia achieved by each basic cycle length was identical at 96%, the other 4% being unwanted arrhythmias (see later). Thus, it took four, five and seven extrastimuli, respectively, for basic cycle lengths of 400 and 600 ms and sinus rhythm to achieve

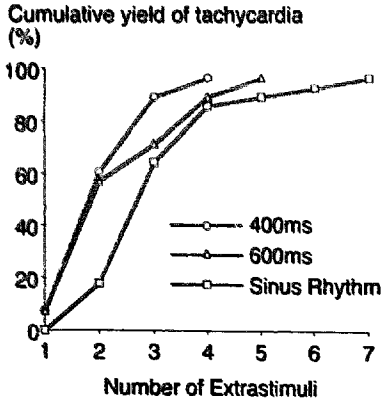
Table 3. Coupling Intervals of Each Extrastimulus Required to Induce Tachycardia in Each Patient

Pt No.	Basic Cycle Length: Sinus Rhythm								600 ms						400 ms				
	SR	S_1S_2	S_2S_3	S_3S_4	S_4S_5	S_5S_6	S_6S_7	S_7S_8	S_1S_1	S_1S_2	S_2S_3	S_3S_4	S_4S_5	S_5S_6	S_1S_1	S_1S_2	S_2S_3	S_3S_4	S_4S_5
1	600	300	250	190	210				580	260	210	280*			400	240	180	200	
2	580	320	280	250					500	280	260	300			400	310	290		
3	600	230	180	220					550	220	230				400	210	210		
4	1060	370	290						600	290	220				400	270	240		
5†	580	260	170	250					600	220	190				400	200	220		
6	600	270	230	180	290				600	240	170	220			400	220	210		
7	540	260	200	210					500	250	210				400	230	190		
8	850	260	240						600	280					400	220			
9	740	300	270	240	210	200	300		600	270	210	230	200	210	400	250	200	170	
10	690	270	270						600	260					400	260			
11	710	270	230						600	270	260				400	240	300		
12†	565	230	200	160	200*				500	240	160	160	170*		400	220	150	200*	
13	720	270	240	270					500	260	300				400	270	220		
14	1200	310	290	270					600	280	210	220	280		400	260	180	280	
15	660	300	230	210	190	190			600	280	220	200	190		400	240	190	190	250
16	620	230	280						550	230	270				400	220	250		
17	880	350	280	220	270				600	300	210	190	250		400	270	180	250	
18	590	240	190	260					500	220	230				400	210	180*		
19	690	280	220	300					600	270	270				400	230	270		
20	670	300	250	200	260				600	270	220	270			400	250	200	260	
21	930	330	260	200	240				600	280	250				400	240	270		
22†	930	340	240	290					600	270	260				400	220	300		
23	670	270	230	200					600	250	200				400	220	220		
24	550	240	210	170	210*				550	240	180	170	300		400	230	170	260	
25	630	250	240	270					600	260	230				400	230	210		
26	800	250	210	270					600	220	300				400	200	290		
27†	500	250	230	200	180	170	170	190*	450	240	180	170	150	290*	400	230	170	160	160*
28†	560	230	230	280*					500	230	210	250*			400	220	190	300*	

*Sustained polymorphic ventricular tachycardia/ventricular fibrillation induced. †Presenting arrhythmia was ventricular fibrillation with cardiac arrest. Pt = patient; S_1S_1 = cycle length of the basic drive; S_1S_2, S_2S_3, S_3S_4, S_4S_5, S_5S_6, S_6S_7, S_7S_8 = coupling intervals of 1st, 2nd, 3rd, 4th, 5th, 6th and 7th extrastimuli, respectively.

maximal inducibility of ventricular tachycardia. 3) As a general rule, the addition of each extrastimulus was roughly as potent as shortening the basic cycle length from sinus rhythm to ventricular pacing at a basic cycle length of 400 ms.

Figure 1. Cumulative yield of clinical tachycardia using 400 and 600 ms and sinus rhythm as the basic cycle lengths. It took four, five and seven extrastimuli, respectively, for basic cycle lengths of 400 and 600 ms and sinus rhythm to achieve maximal inducibility of tachycardia. For every number of extrastimuli used, the yield was higher when the basic cycle length was 400 ms.



Although only 2 patients required four extrastimuli to induce tachycardia when a basic cycle length of 400 ms was used, 7 patients (25%) and 10 patients (36%), respectively, required four or more extrastimuli to induce tachycardia when basic cycle lengths of 600 ms and sinus rhythm were used (Table 3). Thus, the use of at least four extrastimuli is important if conventional basic cycle lengths are used. Restriction of the maximal number of extrastimuli to four yields inducibility rates of 89% and 86% for basic cycle lengths of 600 ms and sinus rhythm, respectively. Restriction of the maximal number of extrastimuli to five yields inducibility rates of 96% and 89% for basic cycle lengths of 600 ms and sinus rhythm, respectively.

Induced arrhythmias. Sustained monomorphic ventricular tachycardia was induced in 72 (86%) of the 84 inductions. Sustained polymorphic ventricular tachycardia/ventricular fibrillation was induced in the remaining 12 inductions (14%). The mean duration of induced arrhythmia was 40 ± 4 s. Direct current countershock was required for arrhythmia termination in 24 (29%) and pace termination in 53 (63%) of

the inductions. In the seven (8%) remaining inductions (one induction in each of seven patients), tachycardia terminated spontaneously after a mean duration of 16 ± 2 s. Each of these patients had sustained monomorphic ventricular tachycardia, cycle length ≥200 ms and lasting >30 s or requiring intervention in the other two inductions.

There were no statistically significant differences in the mean cycle lengths of ventricular tachycardia induced between the use of basic cycle lengths of sinus rhythm (284 ± 82 ms) or right ventricular pacing at 600 ms (278 ± 54 ms) or at 400 ms (270 ± 54 ms).

Induction of unwanted arrhythmias. Sustained polymorphic ventricular tachycardia/ventricular fibrillation was induced in six patients (Table 3). In three of these patients, ventricular fibrillation associated with cardiac arrest was the presenting clinical arrhythmia and ventricular fibrillation was induced at all three inductions in each patient. The induced ventricular fibrillation was considered to be clinical in these three patients. In the other three patients, each had ventricular fibrillation induced during only one of the three inductions. The associated basic cycle length was 400 ms in one patient, 600 ms in another and sinus rhythm in the third. In each of these three patients the presenting clinical arrhythmia was sustained monomorphic ventricular tachycardia, and this arrhythmia was inducible at the other two inductions. The induced polymorphic ventricular tachycardia/ventricular fibrillation was considered an unwanted arrhythmia in these three patients. The incidence of unwanted arrhythmia was therefore identical at 4% for each of the basic cycle lengths. These were induced at the fourth, third and second extrastimuli at basic cycle lengths of sinus rhythm and 600 and 400 ms, respectively.

Extrastimulus coupling intervals. The minimal coupling intervals for each extrastimulus are listed under the three basic cycle lengths for each patient in Table 3. A coupling interval ≤200 ms for at least one extrastimulus was common. Twenty-seven (32%) of 84 inductions involved the use of extrastimulus coupling intervals of <200 ms.

Mean coupling interval of the extrastimulus that induced VT. The coupling intervals of the *last* extrastimulus that induced ventricular tachycardia were similar for each of the three basic cycle lengths (250 ± 35, 249 ± 38 and 239 ± 41 ms for basic cycle lengths of sinus rhythm and 600 and 400 ms, respectively, p = NS).

Effect of multiple extrastimuli and basic cycle lengths on ventricular refractoriness. The mean effective refractory period ± SE for each extrastimulus are shown for the different basic cycle lengths in Figure 2. As expected, effective refractory periods were shortened with additional extrastimuli. Use of a shorter basic cycle length results in earlier shortening of refractory periods. With a longer basic cycle length, more extrastimuli were required to shorten refractory periods. Thus, it took four extrastimuli to shorten the refractory period to a mean of 183 ms when sinus rhythm was used as the basic cycle length, three extrastimuli to shorten it to a mean of 181 ms when 600 ms was used as the basic cycle length and two extrastimuli to shorten it to a mean of 172 ms when 400 ms was used as the basic cycle length.

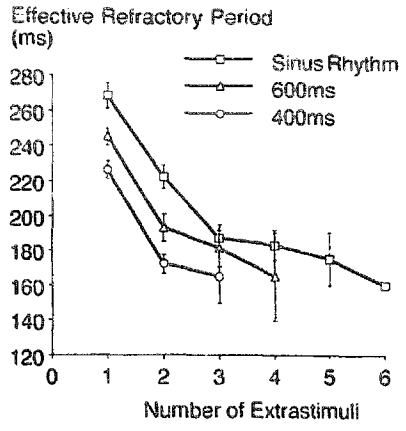


Figure 2. Mean effective refractory period ± SE for each extrastimulus using different basic cycle lengths.

Requirement for direct current countershock. Direct current countershock was required to terminate 24 tachyarrhythmias in 13 patients (Table 2). There was no significant difference in the incidence of direct current countershock requirement at the different basic cycle lengths. Induction of tachycardia earlier in the same electrophysiologic session did not alter the requirement for direct current countershock in subsequent induced tachycardias in the same patient.

Discussion

Although programmed stimulation for ventricular tachycardia is a standard technique that has been available for 20 years, there is an extraordinary lack of uniformity in the stimulation protocols used in different laboratories. Many centers use multiple basic cycle lengths and three or fewer extrastimuli in the belief that a more graduated protocol of stimulation has a higher sensitivity and is associated with a lower incidence of induction of nonclinical ventricular tachycardia/ventricular fibrillation (10,14). This study examined the effects of using different basic cycle lengths for induction of ventricular tachycardia/ventricular fibrillation. Basic cycle lengths of sinus rhythm and 600 and 400 ms were chosen for this study because these represent the range of basic cycle lengths that are conventionally used during clinical electrophysiologic tests. A basic cycle length of <400 ms was not used because of the possibility that myocardial ischemia might be induced. By removing the conventional upper limit of three or four extrastimuli used in previous studies, the true yield of tachycardia with variation in basic cycle lengths could be ascertained and the effects on induction of unwanted arrhythmias noted.

Argument for adding extrastimuli. Several studies have shown an increased yield of clinical tachycardia with the use of three and four extrastimuli (2,3,5,6,15). A common con-

cern is the increased induction of nonclinical arrhythmia (2,6). However, the present study showed that the incidence of induction of polymorphic ventricular tachycardia/ventricular fibrillation was low in patients with documented ventricular tachycardia despite use of more than five or six extrastimuli in some cases. Buxton et al. (2) found that polymorphic ventricular tachycardia or ventricular fibrillation was not more frequently induced by triple extrastimuli than by single or double extrastimuli in patients with documented spontaneous and inducible sustained monomorphic ventricular tachycardia. Our results also demonstrate that the use of up to seven extrastimuli in a stimulation protocol does not impair the specificity of programmed ventricular stimulation in this subgroup of patients.

However, when an aggressive stimulation protocol with up to seven extrastimuli is used in patients without previously documented ventricular tachycardia/ventricular fibrillation (for example, patients without previous myocardial infarction studied because of syncope), the incidence of inducible ventricular fibrillation may be increased. This is a different problem. Such a group of patients has a relatively low incidence of underlying ventricular tachycardia and requires a stimulation protocol with high specificity. Conversely, patients with ECG-documented ventricular tachycardia due to myocardial infarction require a stimulation protocol that has a high sensitivity and allows quantification of baseline variability in ventricular tachycardia induction so that the true effects of antiarrhythmic drugs on inducibility can be assessed at subsequent electrophysiologic studies. Such a protocol may be useful for serial pharmacologic testing, although the present study has not validated the role of this particular protocol for pharmacologic trials.

We did not limit the shortest coupling interval that could be used. One study (16) suggested that less unwanted ventricular fibrillation or polymorphic ventricular tachycardia would be induced by restricting extrastimulus coupling intervals. However, the investigators (16) studied two different patient groups, one with and one without documented spontaneous and inducible monomorphic ventricular tachycardia, rather than comparing shorter coupling intervals within the same group. Naturally, lower coupling intervals were reached and more extrastimuli were used in the group with no spontaneous or inducible tachycardia than those who had inducible tachycardia. On the basis of that report, other groups (9,12) restricted coupling intervals to a minimum of 200 ms. In our study, 27 of 84 inductions involved the use of extrastimulus coupling intervals of <200 ms (Table 3). The coupling interval of the last extrastimulus was <200 ms in only one of the three unwanted arrhythmias induced. This finding is in accord with a recent study that concludes that there is a large overlap in coupling intervals that induced ventricular fibrillation or ventricular tachycardia and that no cutoff can be identified (17).

Argument for repeating stimulation with different basic cycle lengths. Laboratories that use multiple basic cycle lengths (4,10) have suggested that induction of nonclinical ventricular tachycardia occurs less frequently with the use of a maximum of two extrastimuli and multiple basic cycle lengths than with the use of three extrastimuli at one basic cycle length. Several studies (3,4) showed that the cumulative yield of induced ventricular tachycardia with single and double extrastimuli during ventricular pacing increased with the use of multiple decremental basic cycle lengths. However, because of the sequential nature of these protocols, the true yield of the shorter basic cycle length alone versus repetition of previously unsuccessful extrastimuli could not be determined. The effect of repetition of previously unsuccessful extrastimuli is significant and must be taken into account (13).

Our study showed that when a sufficient number of extrastimuli were used, the maximal yield of ventricular tachycardia achieved by each basic cycle length was identical at 96%, although at any given number of extrastimuli up to the fourth extrastimulus, the yield of ventricular tachycardia was higher with a shorter basic cycle length than with a longer basic cycle length. The use of additional extrastimuli at the longer basic cycle length was not associated with increased induction of unwanted arrhythmias. Addition of extrastimuli is as potent as shortening the basic cycle length and saves time compared with repeating the whole protocol at a different basic cycle length.

Because the shortest basic cycle length facilitates induction of ventricular tachycardia without increasing the incidence of unwanted arrhythmias, a basic cycle length of 400 ms should become the standard basic cycle length for programmed stimulation protocols for ventricular tachycardia induction. Basic cycle lengths of <400 ms were not tested in this study and may yield even better results. However, pacing-induced ischemia may be a problem in this group of patients if a rapid basic cycle length is used. Morady et al. (18) recently concluded that use of a short basic cycle length (350 ms) and three extrastimuli improved the efficiency and specificity of programmed stimulation without impairing the yield of monomorphic ventricular tachycardia. Obviously, the stimulation protocol is completed more quickly if the basic cycle length is shorter, thus saving time. Another advantage of a short basic cycle length is the more reliable ventricular capture in the drive train with less interference from sinus tachycardia or spontaneous atrial and ventricular ectopic beats.

In our study, only one patient had ventricular tachycardia induced with fewer extrastimuli with a longer basic cycle length versus a shorter basic cycle length. This observation suggests that repeating stimulation with a longer basic cycle length after a short basic cycle length has been unsuccessful is unlikely to induce ventricular tachycardia. The effects of repetition of the same protocol on the increasing yield of tachycardia were minimized in our study by repeating each extrastimulus coupling interval three times before decreasing the interval. Any increase in yield observed in previous studies when the drive chain is changed to a longer basic

cycle length is probably related to the effect of simply repeating the same stimulation protocol.

Ventricular effective refractory periods. There is an inverse relation between heart rate and refractoriness in human ventricular myocardium (19,20). Our study showed that earlier achievement of the maximal yield of ventricular tachycardia with shorter drive cycle lengths was associated with earlier achievement of shorter ventricular refractory periods for each extrastimulus. However, use of an adequate number of extrastimuli can shorten refractory periods to the same extent if one chooses to use a longer basic cycle length. The effects on shortening refractory periods reached a plateau after three to four extrastimuli, depending on the basic cycle length. Shortening the refractory period allowed premature stimulation to be delivered at shorter coupling intervals. However, once refractoriness was decreased to a certain degree, the coupling interval of the final extrastimulus that induced tachycardia was not necessarily short.

Study limitations. We studied only patients with old myocardial infarction and documented ventricular tachycardia/ventricular fibrillation. The findings may not be applicable to patients with other etiologies of ventricular tachycardia. Five patients in this study had ventricular fibrillation rather than ventricular tachycardia as the documented clinical arrhythmia. Our findings would be unchanged if these five patients were eliminated from analysis.

Conclusions. The use of an adequate number of extrastimuli obviates the need for multiple basic cycle lengths for induction of ventricular tachycardia and does not increase induction of unwanted ventricular fibrillation. If only one basic cycle length is used, the ease of inducibility can be quantified in terms of the number of extrastimuli required. Fewer extrastimuli were required for induction of ventricular tachycardia if a basic cycle length of 400 ms was used. These data favor the use of ventricular pacing at a basic cycle length of 400 ms with up to at least four extrastimuli as the standard stimulation protocol for induction of ventricular tachycardia.

References

1. Zipes DA, Akhtar M, Denes P, et al. Guidelines for clinical intracardiac electrophysiologic studies. A report for the American College of Cardiology/American Heart Association Task Force on assessment of diagnostic and therapeutic cardiovascular procedures (subcommittee to assess clinical intracardiac electrophysiologic studies). J Am Coll Cardiol 1989; 14:1827–42.
2. Buxton AE, Waxman HL, Marchlinski FL, Untereker WJ, Waspe LE, Josephson ME. Role of triple extrastimuli during electrophysiologic study of patients with documented sustained ventricular tachyarrhythmias. Circulation 1984;69:532–40.
3. Brugada P, Wellens HJJ. Comparison in the same patient of two programmed ventricular stimulation protocols to induce ventricular tachycardia. Am J Cardiol 1985;55:380–3.
4. Estes M, Garan H, McGovern B, Ruskin JN. Influence of drive cycle length during programmed stimulation on induction of ventricular arrhythmias: analysis of 403 patients. Am J Cardiol 1986;57:108–12.
5. Lin HT, Mann DE, Luck JC, et al. Prospective comparison of right and left ventricular stimulation for induction of sustained ventricular tachycardia. Am J Cardiol 1987;59:559–63.
6. Mann DE, Luck JC, Griffin JC, et al. Induction of clinical ventricular tachycardia using programmed stimulation: value of third and fourth extrastimuli. Am J Cardiol 1983;52:501–6.
7. Morady F, DiCarlo L, Winston S, Davis JC, Scheinman MM. A prospective comparison of triple extrastimuli and left ventricular stimulation in studies of ventricular tachycardia induction. Circulation 1984;70:52–7.
8. Morady F, Kou WH, Kadish AH, Schmaltz S, Summitt J, Rosenheck S. Effect of basic drive train cycle length on induction of ventricular tachycardia by a single extrastimulus. J Electrophysiol 1989;3:111–6.
9. Summitt J, Rosenheck S, Kou WH, Schmaltz S, Kadish AH, Morady F. Effect of basic cycle length on the yield of ventricular tachycardia during programmed ventricular stimulation. Am J Cardiol 1990;65:49–52.
10. Breithardt G, Borggrefe M, Podczeck A, Budde T. Influence of the cycle length of basic drive on induction of sustained ventricular tachycardia associated with coronary artery disease. Am J Cardiol 1987;60:1306–10.
11. Doherty JU, Kienzle MG, Waxman HL, Buxton AE, Marchlinski FE, Josephson ME. Relation of mode of induction and cycle length of ventricular tachycardia: analysis of 104 patients. Am J Cardiol 1983;52: 60–4.
12. Gillis AM, Winkle RA, Echt DS. Role of extrastimulus prematurity and intraventricular conduction time in inducing ventricular tachycardia or ventricular fibrillation secondary to coronary artery disease. Am J Cardiol 1987;60:590–5.
13. Cooper MJ, Hunt LJ, Richards DA, Denniss AR, Uther JB, Ross DL. Effect of repetition of extrastimuli on sensitivity and reproducibility of mode of induction of ventricular tachycardia by programmed stimulation. J Am Coll Cardiol 1988;11:1260–7.
14. Doherty JU, Kienzle MG, Waxman HL, Buxton AE, Marchlinski FE, Josephson ME. Programmed ventricular stimulation at a second right ventricular site: an analysis of 100 patients, with special reference to sensitivity, specificity and characteristics of patients with induced ventricular tachycardia. Am J Cardiol 1983;52:1184–9.
15. Herre JM, Mann DE, Luck JC, et al. Effect of increased current, multiple pacing sites and number of extrastimuli on induction of ventricular tachycardia. Am J Cardiol 1986;57:102–7.
16. Morady F, DiCarlo LA, Baerman JM, de Buitleir M. Comparison of coupling intervals that induce clinical and nonclinical forms of ventricular tachycardia during programmed stimulation. Am J Cardiol 1986;57:1269–73.
17. Avitall B, McKillie J, Jazayeri M, Akhtar M, Anderson AJ, Tchou P. Induction of ventricular fibrillation versus monomorphic ventricular tachycardia during programmed stimulation. Role of premature beat conduction delay. Circulation 1992;85:1271–8.
18. Morady F, Kadish A, deButtleir M, et al. Prospective comparison of a conventional and an accelerated protocol for programmed ventricular stimulation in patients with coronary artery disease. Circulation 1991;83: 764–73.
19. Guss SB, Kastor JA, Josephson ME, Scharf DL. Human ventricular refractoriness. Effects of cycle length, pacing site and atropine. Circulation 1976;53:450–5.
20. Denes P, Wu D, Dhingra R, Pietras RJ, Rosen KM. The effects of cycle length on cardiac refractory periods in man. Circulation 1974;49:32–41.